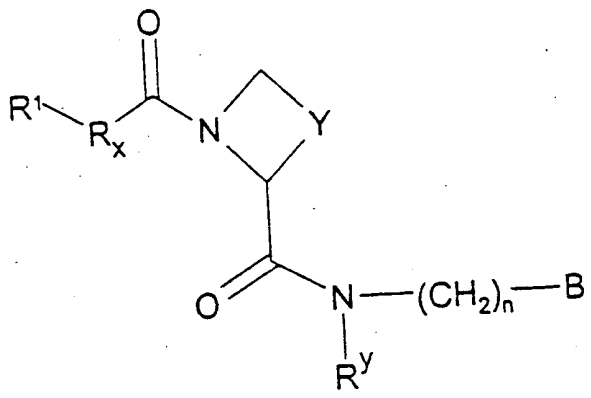
**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1 (currently amended). A compound of formula I,



I

wherein

$R^1$ represents H, $C_{1-4}$ alkyl (optionally substituted by one or more substituents selected from cyano, halo, OH, $C(O)OR^{1a}$ or $C(O)N(R^{1b})R^{1c}$) or $OR^{1d}$;

$R^{1d}$ represents H, $C(O)R^{11}$, $SiR^{12}R^{13}R^{14}$ or $C_{1-6}$ alkyl, which latter group is optionally substituted or terminated by one or more substituent selected from $OR^{15}$ or $(CH_2)_qR^{16}$;

$R^{12}$, $R^{13}$ and $R^{14}$ independently represent H, phenyl or $C_{1-6}$ alkyl;

$R^{16}$ represents $C_{1-4}$ alkyl, phenyl, OH, $C(O)OR^{17}$ or $C(O)N(H)R^{18}$;

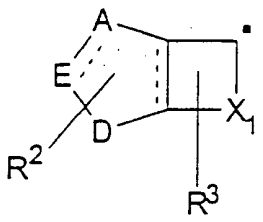
$R^{18}$ represents H, $C_{1-4}$ alkyl or $CH_2C(O)OR^{19}$;

$R^{15}$ and $R^{17}$ independently represent H, $C_{1-6}$ alkyl or $C_{1-3}$ alkylphenyl;

$R^{1a}$, $R^{1b}$, $R^{1c}$, $R^{11}$ and $R^{19}$ independently represent H or $C_{1-4}$ alkyl; and

q represents 0, 1 or 2;

$R_x$ represents a structural fragment of formula IIa,




IIa

wherein

the dotted lines independently represent optional bonds;

A and E independently represent CH;

D represents ~~$-CH_2-$, O, S, $N(R^{22})$, $-(CH_2)_2-$,~~ -CH=CH-, ~~$-CH_2N(R^{22})-$, $-N(R^{22})CH_2-$, -CH=N-, -N=CH-, $-CH_2O-$, $-OCH_2-$, $-CH_2S-$ or $-SCH_2-$~~;

$X_1$ represents $-Z-A^3$;

$A^3$ represents $C_{1-3}$ alkylene;

Z represents~~, at each occurrence,~~ $S(O)_m$;

$R^2$ represents one or more optional substituents selected from $C_{1-4}$ alkyl, $C_{1-4}$ alkoxy (which latter two groups are optionally substituted by one or more halo substituent), methylenedioxy, halo, hydroxy, cyano, nitro, $S(O)_2NH_2$, $C(O)OR^{26}$, $SR^{26}$, $S(O)R^{26a}$, $S(O)_2R^{26a}$ or $N(R^{27})R^{28}$;

$R^3$ represents one or more optional substituents selected from OH, $C_{1-4}$ alkoxy, $C_{1-6}$ alkyl (optionally substituted by one or more halo group), or $N(R^{29a})R^{29b}$;

~~$R^{25}$~~, $R^{29a}$ and $R^{29b}$ independently represent H, $C_{1-4}$ alkyl or $C(O)R^{30}$;

$R^{26}$ represents H or $C_{1-4}$ alkyl;

$R^{26a}$ represents $C_{1-4}$ alkyl;

$R^{27}$ and $R^{28}$ independently represent H, $C_{1-4}$ alkyl or $C(O)R^{30}$, or together represent $C_{3-6}$ alkylene, thus forming a 4- to 7-membered ring, which ring is optionally substituted, on a carbon atom that is $\alpha$ to the nitrogen atom, with an =O group;

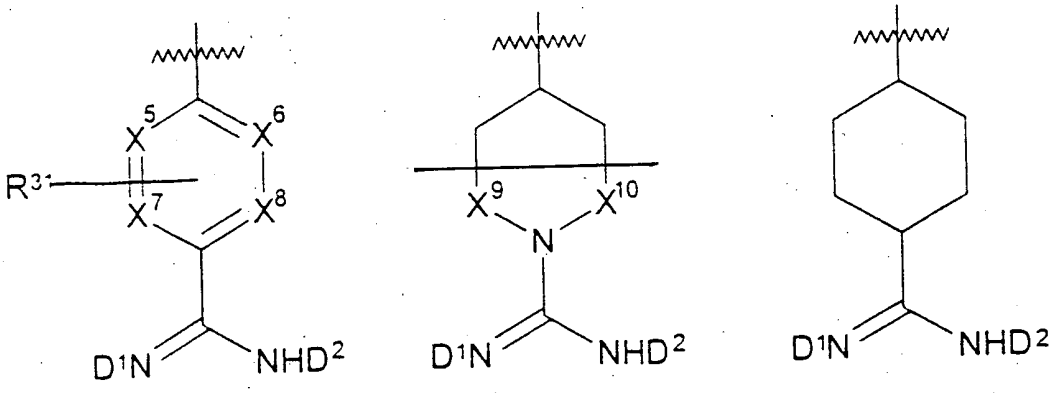
~~$R^{21}$, $R^{22}$, $R^{23}$, $R^{24}$ and~~ $R^{30}$ ~~independently represent~~ represents, at each occurrence, H or $C_{1-4}$ alkyl;

Y represents $CH_2$, $(CH_2)_2$, or CH = CH ~~(which latter group is optionally substituted by $C_{1-4}$ alkyl), $(CH_2)_3$, $CH_2CH=CH$ or $CH=CHCH_2$ (which latter three groups are optionally substituted by $C_{1-4}$ alkyl, methylene, =O or hydroxy)~~;

$R^y$ represents H or $C_{1-4}$ alkyl;

n represents 0, 1, 2, 3 or 4; and

B represents a structural fragment of formula IIIa~~, IIIb~~ or IIIc




IIIa IIIb IIIc

wherein

$X^5$, $X^6$, $X^7$ and $X^8$ independently represent CH~~, N or N-O~~;

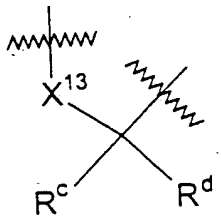
~~$X^9$ and $X^{10}$ independently represent a single bond or $CH_2$;~~

$R^{31}$ represents an optional substituent selected from halo, $C_{1-4}$ alkyl (which group is optionally substituted by one or more halo group), $N(R^{32})R^{33}$, $OR^{34}$ or $SR^{35}$;

$R^{32}$ and $R^{33}$ independently represent H, $C_{1-4}$ alkyl or $C(O)R^{36}$;

$R^{34}$, $R^{35}$ and $R^{36}$ independently represent H or $C_{1-4}$ alkyl; and

one of $D^1$ and $D^2$ represents H, and the other represents H, $OR^a$, $NHR^a$, $C(=X^{11})X^{12}R^b$, or $D^1$ and $D^2$ together represent a structural fragment of formula IVa:-




IVa

$R^a$ represents H or $-A^5[X^{14}]_n[C(O)]_rR^e$;

$R^b$ represents $-A^5[X^{14}]_n[C(O)]_rR^e$;

$A^5$ represents, at each occurrence, a single bond or $C_{1-12}$ alkylene (which alkylene group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group, and is optionally substituted by one or more of halo, OH, $N(H)C(O)R^g$, $C(O)N(R^g)R^h$, $C_{3-7}$-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group and/or is optionally substituted by one or more substituents selected from $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, halo, =O or =S), Het and $C_{6-10}$ aryl (which aryl and Het groups are themselves optionally substituted by one or more substituents selected from $C_{1-6}$ alkyl (optionally substituted by one or more halo substituent), $C_{1-6}$ alkoxy, halo, cyano, $C(O)OR^g$, $C(O)N(R^g)R^h$ and $N(R^f)R^g$));

$R^c$ and $R^d$ both represent H; or one of $R^c$ and $R^d$ represents H or $C_{1-7}$ alkoxy and

the other represents $C_{1-17}$ alkyl (which alkyl group is optionally interrupted by one or more O atoms); or $R^c$ and $R^d$ together represent $C_{3-8}$ cycloalkyl, which cycloalkyl group is interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group;

$R^e$ represents, at each occurrence, H, $C_{1-12}$ alkyl (which alkyl group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group, and/or is optionally substituted by one or more substituents selected from halo, OH, $N(H)C(O)R^g$ and $C(O)N(R^g)R^h$), $A^7$-$C_{3-7}$-cycloalkyl (which cycloalkyl group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group and/or is substituted by one or more substituents selected from $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, halo, =O and =S), $A^7$-$C_{6-10}$ aryl or $A^7$-Het (which aryl and Het groups are optionally substituted by one or more substituents selected from $C_{1-6}$ alkyl (optionally substituted by one or more halo substituent), $C_{1-6}$ alkoxy, halo, cyano, $C(O)OR^g$, $C(O)N(R^g)R^h$ and $N(R^f)R^g$);

$A^7$ represents a single bond or $C_{1-7}$ alkylene (which alkylene group is optionally interrupted by one or more O, $S(O)_m$ and/or $N(R^f)$ group, and/or are optionally substituted by one or more of halo, OH, $N(H)COR^g$ and $CON(R^g)R^h$);

Het represents, at each occurrence, a five- to ten-membered heteroaryl group, which may be aromatic in character, containing one or more nitrogen, oxygen or sulphur atoms in the ring system;

n and r independently represent 0 or 1;

$X^{11}$, $X^{12}$ and $X^{14}$ independently represent O or S;

$X^{13}$ represents O or $N(R^f)$;

$R^f$ represents, at each occurrence, H, $C_{1-4}$ alkyl or $C(O)R^g$;

~~$R_g$~~ $R^g$ and $R^h$ independently represent, at each occurrence, H or $C_{1-4}$ alkyl; and

m represents, at each occurrence, 0, 1 or 2;

or a pharmaceutically acceptable salt thereof;

provided that:

(a) when $A^5$ represents a single bond, then n and r both represent 0;

(b) when $A^5$ represents $C_{1-12}$ alkylene, then n represents 1;

(c) when $A^5$ represents $-CH_2-$, n is 1 and r is 0, then $R^e$ does not represent H; and

(d) the compound is not:-

*(S)*- or *(R)*-1 -hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

*(R)*- or *(S)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Pro-Pab;

*(S)*- or (R)-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

*(R)*- or *(S)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab;

1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

1-hydroxy-5,7-dimethyltetralin-1-yl-C(O)-Aze-Pab x HOAc;

1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab x HOAc;

1-hydroxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

*(R)*- or (S)-7-methoxy-1-methyltetralin-1-yl-C(O)-Aze-Pab;

4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x OAc;

*(S)*- or *(R)*-1-hydroxy-4-methoxyindan-1-yl-C(O)-Aze-Pab;

1-hydroxy-5-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);

(*S*)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(OH);

4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OH);

4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab(OMe);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-

(C(O)$OCH_2CCl_3$);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-

(C(O)$OCH_2CH_3$);

7-methoxy-1-allyltetralin-1-yl-C(O)-Aze-Pab x HOAc;

*(S)*- or *(R)*-1-hydroxy-7-chlorotetralin-1-yl-C(O)-Pro-Pab;

1-*n*-propyl-7-methoxytetralin-1-yl-C(O)-Aze-Pab x HOAc;

6-chloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

6,8-dichloro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

6-fluoro-4-hydroxychroman-4-yl-C(O)-Aze-Pab x HOAc;

4-hydroxy-6-methylchroman-4-yl-C(O)-Aze-Pab x HOAc;

8-chloro-4-hydroxy-6-methoxychroman-4-yl-C(O)-Aze-Pab x HOAc;

6-chloro-4-hydroxy-8-methylcbroman-4-yl-C(O)-Aze-Pab x HOAc;

(*S*)- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-*i*-Pr);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Et);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-C(O)-Ch);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-allyl);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(0-Bzl);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab-

(CO-O-methallyl);

1-hydroxy-7-aminotetralin-1-yl-C(O)-Aze-Pab(OH);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-Pab(O-Val);

*(S)*- or *(R)*-1-hydroxy-7-methoxytetralin-1-yl-C(O)-Aze-(Me)Pab; or

9-hydroxyfluoren-9-yl-C(O)-Aze-Pab x HOAc.

2 (original). A compound as claimed in Claim 1 wherein $R^1$ represents OH or $C_{1-4}$ alkyl (which latter group is optionally substituted by cyano or OH).

3 (canceled).

4 (currently amended). A compound as claimed in claim 1 wherein~~, when~~ the dotted lines in the structural fragment of formula II represent bonds~~, D represents -CH=CH-~~.

5 (currently amended). A compound as claimed in claim 1 wherein $A^3$ represents $C_1$- or $C_2$-alkylene ~~which latter group is optionally unsaturated~~.

6 (currently amended). A compound as claimed in claim 1 wherein Y represents $CH_2$~~,~~ or $(CH_2)_2$ ~~or $(CH_2)_3$~~.

7 (previously presented). A compound as claimed in claim 1 wherein B represents a structural fragment of formula IIIa in which $X^5$, $X^6$, $X^7$ and $X^8$ all represent CH.

8 (previously presented). A compound as claimed in claim 1 wherein, when $D^1$

and $D^2$ together represent a structural fragment of formula IVa, in which $X^{13}$ is O, then one of $R^c$ and $R^d$ represents H or $C_{1-7}$ alkoxy and the other represents $C_{1-7}$ alkyl.

9 (previously presented). A compound as claimed in claim 1, wherein, when $D^1$ or $D^2$ represents $OR^a$ and $R^a$ represents $-A^5[X^{14}]_n[C(O)]_rR^e$, and

(i) $A^5$ is a single bond, then $R^e$ is:-

(1) $A^7$-aryl, optionally substituted by one or more halo, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl or halo-$C_{1-6}$-alkyl substituents; or

(2) H or linear, branched, optionally unsaturated, and/or cyclic, $C_{1-12}$ alkyl, which cyclic alkyl group is optionally interrupted by an O atom and, optionally, a further O atom or $S(O)_m$ group; or when

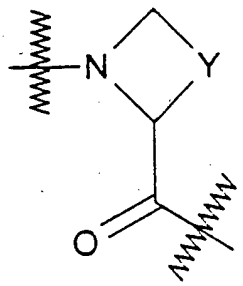
(ii) $A^5$ is linear or branched $C_{1-12}$ alkylene, $X^{14}$ is O and r is 0, then $R^e$ is $C_{1-3}$ alkyl or $A^7$-aryl, in which $A^7$ is a single bond.

10 (previously presented). A compound as claimed in claim 1, wherein, when $D^1$ or $D^2$ represents $OR^a$, then $R^a$ is H or $C_{1-4}$ alkyl.

11 (previously presented). A compound as claimed in claim 1, wherein, when $D^1$ or $D^2$ represents $-C(=X^{11})X^{12}R^b$, in which $X^{11}$ represents O and $X^{12}$ represents O or S, and, in which $R^b$ group, $A^5$ represents a single bond then $R^e$ represents optionally unsaturated $C_{1-6}$ alkyl, $A^7$-$C_{6-10}$-aryl (in which $A^7$ represents a single bond or $C_{1-2}$ alkylene, and which $A^7$-$C_{6-10}$-aryl group is optionally substituted by one or more halo, $C_{1-4}$ alkyl and/or $C_{1-4}$ alkoxy groups), or $A^7$-$C_{3-7}$-cycloalkyl, in which $A^7$ represents a single

bond or linear or branched $C_{1-7}$ alkylene, and which cycloalkyl group is optionally substituted by $C_{1-3}$ alkyl.

12 (previously presented). A compound of formula I, as defined in claim 1, wherein the fragment




is in the S-configuration.

13 (previously presented). A pharmaceutical formulation including a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

14-20 (canceled).

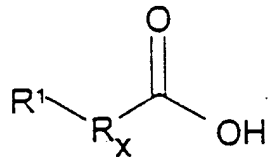
21 (previously presented). A method of treatment of a condition where inhibition of thrombin is required which method comprises administration of a therapeutically effective amount of a compound as defined in claim 1, or a pharmaceutically acceptable salt thereof, to a person suffering from, or susceptible to, such a condition.

22 (original). A method as claimed in Claim 21, wherein the condition is thrombosis.

23 (original). A method as claimed in Claim 21, wherein the condition is hypercoagulability in blood and tissues.

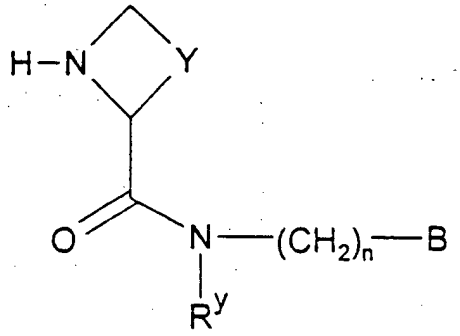
24 (original). A process for the preparation of compounds of formula I which comprises:

(i) the coupling of a compound of formula IV,



IV

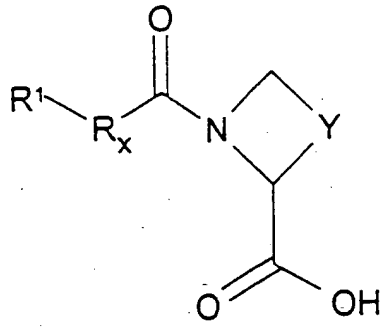
wherein $R^1$ and $R_x$ are as defined in Claim 1 with a compound of formula V,



V

wherein $R^y$, Y, n and B are as defined in Claim 1;

(ii) the coupling of a compound of formula VI,



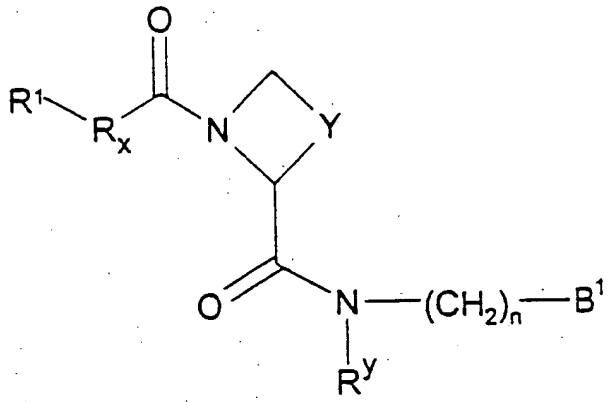
VI

wherein $R^1$, $R_x$ and Y are as defined in Claim 1 with a compound of formula VII,

$$H(R^y)N\text{-}(CH_2)_n\text{-}B \qquad \text{VII}$$

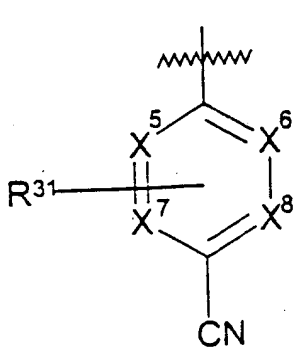
wherein $R^y$, n and B are as defined in Claim 1;

(iii) for compounds of formula I in which $D^1$ or $D^2$ represents $OR^a$ or $NHR^a$, reaction of a compound of formula VIII,

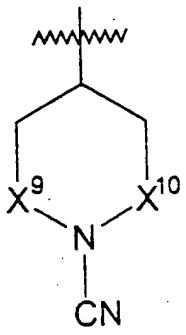


VIII

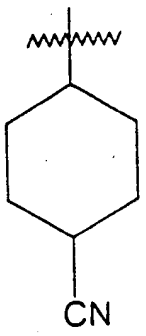
wherein $B^1$ represents a structural fragment of formula IIId, IIIe or IIIf




IIId




IIIe




IIIf

and $R^1$, $R_x$, Y, $R^y$, n, $R^{31}$, $X^5$, $X^6$, $X^7$, $X^8$, $X^9$ and $X^{10}$ are as defined in Claim 1 with a compound of formula IX,

$$H_2NX^aR^a \qquad IX$$

wherein $X^a$ represents O or NH and $R^a$ is as defined in Claim 1;

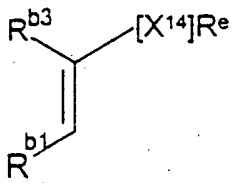
(iv) for compounds of formula I in which $D^1$ or $D^2$ represents $OR^a$ or $NHR^a$, reaction of a compound of formula I in which $D^1$ or $D^2$ (as appropriate) represents $C(O)OR^{b1}$, in which $R^{b1}$ represents a protecting group with a compound of formula IX as defined above;

(v) for compounds of formula I in which $D^1$ or $D^2$ represents $OR^a$ or $NHR^a$, $R^a$ represents $-A^5[X^{14}]_n[C(O)]_rR^e$, in which $A^5$ does not represent a single bond, and n represent 1, reaction of a compound of formula I in which $D^1$ or $D^2$ (as appropriate) represents OH or $NH_2$, with a compound of formula X,

$$L^1A^{5a}[X^{14}][C(O)]_rR^e \qquad X$$

wherein $L^1$ represents a suitable leaving group, $A^{5a}$ represents $A^5$, as defined in Claim 1 except that it does not represent a single bond, and $X^{14}$, r and $R^e$ are as defined in Claim 1;

(vi) for compounds of formula I in which $D^1$ or $D^2$ represents $OR^a$ or $NHR^a$, $R^a$ represents $-A^5[X^{14}]_n[C(O)]_rR^e$, in which $A^5$ represents $C_{2-12}$ alkylene, which alkylene group is branched at the carbon atom that is $\alpha$ to the O or N atom of $OR^a$ or $NHR^a$ (as appropriate), and which group is optionally branched at the carbon atom that is $\beta$ to that atom, n represents 1, r represents 0 and $R^e$ is as defined in Claim 1, reaction of a compound of formula I in which $D^1$ or $D^2$ (as appropriate) represents OH or $NH_2$, with a compound of formula XI,

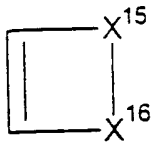


XII

or a geometrical isomer thereof, or a mixture of such geometrical isomers, in which $R^{b1}$ and $R^{b3}$ each represent H or an alkyl group, provided that the total number of carbon atoms provided by $R^{b1}$ and $R^{b3}$ does not exceed 10, and wherein $X^{14}$ and $R^e$ are as defined in Claim 1;

(vii) for compounds of formula I in which $D^1$ or $D^2$ represents $OR^a$ or $NHR^a$, represents $-A^5[X^{24}]_n[C(O)]_rR^e$, in which $A^5$ represents a single bond, and $R^e$ represents $A^7$-$C_{3-6}$-cycloalkyl, in which $A^7$ represents a single bond, and the cycloalkyl group is interrupted by at least one O or S atom, which atom is between the carbon atom at the point of attachment to the O or NH group of $OR^a$ or $NHR^a$, and a carbon atom that is $\alpha$

to that point of attachment, and which cycloalkyl group is optionally interrupted by one or more O or $S(O)_m$ group and/or optionally substituted by one or more =O group, reaction of a compound of formula I, in which $D^1$ or $D^2$ (as appropriate) represents OH or $NH_2$, with a compound of formula XII,




XII

wherein $X^{15}$ represents O or S and $X^{16}$ represents $C_{1-4}$ alkylene (which alkylene group is optionally interrupted by one or more O or $S(O)_m$ group and/or optionally substituted by one or more =O group);

(viii) for compounds of formula I in which $D^1$ or $D^2$ represents $C(X^{11})X^{12}R^b$, reaction of a compound of formula I in which $D^1$ and $D^2$ both represent H with a compound of formula XIII,

$$L^2\text{-}C(X^{11})X^{12}R^b \qquad \text{XIII}$$

wherein $L^2$ represents a suitable leaving group, and $X^{11}$, $X^{12}$ and $R^b$ are as defined in Claim 1;

(ix) for compounds of formula I in which $D^1$ and $D^2$ together represent a structural fragment of formula IVa, reaction of a corresponding compound of formula I in which $D^1$ or $D^2$ represents OH or $NHR^f$ (in which $R^f$ is as defined in Claim 1), with a compound of formula XV,

$$(R^c)(R^d)C(R^{c1})(R^{c2}) \qquad \text{XV}$$

wherein $R^{c1}$ and $R^{c2}$ both represent $-OR^{c3}$, in which $R^{c3}$ represents $C_{1-3}$ alkyl, or

together represent =O, and $R^c$ and $R^d$ are as defined in Claim 1;

(x) for compounds of formula I in which one or more of $X^5$, $X^6$, $X^7$ and $X^8$ represent N-O, oxidation of a corresponding compound of formula I in which $X^5$, $X^6$, $X^7$ and/or $X^8$ (as appropriate) represent(s) N; or

(xi) for compounds of formula I in which any one of Z, $X_1$, $R^2$, $R^4$, $A^5$, $A^7$, $R^c$, $R^d$ and/or $R^e$ comprises or includes a (O) or a $S(O)_2$ group, oxidation of a corresponding compound of formula I (or a compound corresponding to a compound of formula I) wherein Z, $X_1$, $R^2$, $R^4$, $A^5$, $A^7$, $R^c$, Rd and/or $R^e$ (as appropriate) comprise(s) or include(s) a S group;

(xii) for compounds of formula I in which $D^1$ and $D^2$ both represent H, removal of a $OR^a$, $NHR^a$ or $C(=X^{11})X^{12}R^b$ group (in which $R^a$, $R^b$, $X^{11}$ and $X^{12}$ are as defined in Claim 1), or removal of a structural fragment of formula IVa as defined in Claim 1, from a corresponding compound of formula I; or

(xiii) introduction and/or interconversion of a substituent on an aromatic and/or non-aromatic, carbocyclic and/or heterocyclic ring in a corresponding compound of formula I.